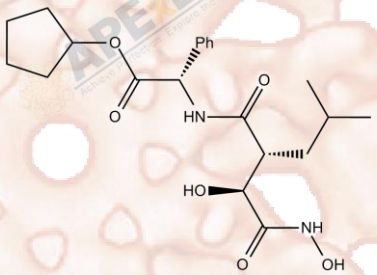
Product Data Sheet

Tosedostat (CHR2797)



Cat. No.: A4355
CAS No.: 238750-77-1
Formula: C21H30N2O6
M.Wt: 406.47
Synonyms:
Target: Metabolism
Pathway: Aminopeptidase
Storage: Store at -20°C

Solvent & Solubility

In Vitro

⩾40.6 mg/mL in DMSO; insoluble in H2O; ⩾15.07 mg/mL in EtOH with ultrasonic

Preparing Stock Solutions

Concentration \ Mass / Solvent	1mg	5mg	10mg
1 mM	2.4602 mL	12.3010 mL	24.6021 mL
5 mM	0.4920 mL	2.4602 mL	4.9204 mL
10 mM	0.2460 mL	1.2301 mL	2.4602 mL

Please refer to the solubility information to select the appropriate solvent.

Biological Activity

Shortsummary	Aminopeptidase inhibitor
IC_{50} & Target	100 nM (LAP), 150 nM (PuSA), 220 nM (Aminopeptidase N)

In Vitro

Cell Viability Assay

Cell Line:	Human multiple myeloma (MM) cells
Preparation method:	The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting conditions:	10 μM, 72 hours

	Applications:	CHR2797 showed antiproliferative and apoptotic effects against MM in vitro by inducing the AA deprivation response (AADR). Using MTS and CTG assays, CHR2797, at clinically achievable concentrations, decreased survival and proliferation in MM1S and IL-6-dependent ANBL6 cells, in the presence or absence of bone marrow stromal cells following 72 hours incubation. CHR2797 induced apoptosis in MM cells via activation of Caspase 3/7 and 9 but not Caspase 8. CHR2797 (10 μM) induced apoptosis in patient MM cells. Combined treatment with CHR2797 and LBH589 in MM cells (MM1S, ANBL6, and INA6) further reduced cell viability following 72 hour incubation when compared with CHR2797 treatment alone. CHR2797 (1 μM) in combination with LBH589 (1 nM) showed an increased growth arrest in G0/G1 cells in MM1R cells treated with both drugs versus CHR2797 alone after 24 hours. CHR2797 inhibited anti-apoptotic protein Mcl-1 in MM1R and U266 MM cells.
In Vivo	**Animal experiment**	
	Dosage form:	60 mg to 180 mg, 28 days, capsules, orally after food each day
	Applications:	Oral once daily dosing with 130 mg tosedostat was well tolerated and had significant antileukemic activity.
	Other notes:	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Product Citations

1.Drinkwater, Nyssa, et al. "X‐ray crystal structures of an orally available aminopeptidase inhibitor, Tosedostat, bound to anti‐malarial drug targets PfA‐M1 and PfA‐M17." Proteins: Structure, Function, and Bioinformatics (2015).PMID:25645579

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References

[1]. Acharya C, Zhong M Y, Tannenbaum D, et al. Targeting Aminopeptidases by Tosedostat (TST)(CHR2797), Alone and with LBH589, Induces Significant Cytotoxicity Against Human Multiple Myeloma (MM) Cells[J]. 2012.

[2]. Lwenberg B, Morgan G, Ossenkoppele G J, et al. Phase I/II clinical study of Tosedostat, an inhibitor of aminopeptidases, in patients with acute myeloid leukemia and myelodysplasia[J]. Journal of Clinical Oncology, 2010, 28(28): 4333-4338.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable

under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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